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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/078,658	02/21/2002	Forrest L. Smith	02940182AA	4757
30743	7590	03/25/2004		
WHITHAM, CURTIS & CHRISTOFFERSON, P.C. 11491 SUNSET HILLS ROAD SUITE 340 RESTON, VA 20190				
EXAMINER JIANG, SHAOJIA A				
ART UNIT		PAPER NUMBER		
1617				

DATE MAILED: 03/25/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 10/078,658	<b>Applicant(s)</b> SMITH ET AL.	
	<b>Examiner</b> Shaojia A Jiang	<b>Art Unit</b> 1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 30 December 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-18 is/are pending in the application.
- 4a) Of the above claim(s) 3,9 and 13-18 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-8 and 10-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

### **DETAILED ACTION**

This Office Action is a response to Applicant's response (remarks) filed on December 30, 2003 wherein no claims have been amended.

### ***Election/Restrictions***

Applicant's affirmation of the telephonic election without traverse of the invention of Group II, Claims 13-18, drawn to composition comprising methanesulfonamide compound and an amide-linked or ester-linked local anesthetic or combinations thereof, and the invention of species ibutilide and bupivacaine, submitted December 30, 2003 is acknowledged.

As recorded in the previous Office Action October 3, 2003, Claims 13-18 withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, and claims 3 and 9 as being drawn to non-elected species.

Claims 1,2, 4-8 and 10-12 are herein examined on the merits in so far as they read on the elected species bupivacaine and ibutilide.

### ***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1, 2, 4-8, and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Sensorcaine with epinephrine entry of the PDR in view of Corevert entry of the PDR for the same reasons of record in the previous Office Action October 3, 2003.

Sensorcaine entry of the PDR teaches a composition employed in a method of inducing local anesthesia. Epinephrine reduces the rate of absorption and peak plasma concentration of bupivacaine, permitting the use of moderately larger total doses and sometimes prolonging the duration of the action. Sensorcaine also teaches that bupivacaine is known to have adverse cardiovascular system reactions such as arrhythmias, cardiac arrest, for example.

Corevert entry of the PDR teaches ibutilide as an antiarrhythmic drug.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate ibutilide in a composition comprising bupivacaine and epinephrine, employed in a method of inducing analgesia.

One of ordinary skill in the art would have been motivated to incorporate ibutilide in a composition comprising bupivacaine and epinephrine, employed in a method of inducing analgesia because bupivacaine has been known to cause systemic cardiovascular effects, e.g., arrhythmia, ventricular fibrillation, cardiac arrest and ibutilide is an agent known for its antiarrhythmic properties.

Therefore the Skilled Artisan would be motivated to incorporate ibutilide into a regimen comprising a composition comprising bupivacaine and

epinephrine in order to lower the incidence of bupivacaine adverse effects, thereby increasing the potency of bupivacaine.

***Response to Argument***

Applicant's remarks filed December 30, 2003 with respect to the rejection made under 35 U.S.C. 103(a) of record in the previous Office Action October 3, 2003 have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant asserts that "there is absolutely no teaching or suggestion concerning the desirability of co-administering an antiarrhythmic agent with a local anesthetic". The examiner acknowledged that the cited prior art does not expressly disclose the incorporation of ibutilide in a composition comprising bupivacaine and epinephrine, employed in a method of inducing analgesia. That was why the rejection is made under 35 U.S.C. 103(a) for obviousness over the prior art, but not under 35 U.S.C. 102(b) for anticipation. As discussed in the previous Office Action, one of ordinary skill in the art would have been motivated to incorporate ibutilide in a composition comprising bupivacaine and epinephrine, employed in a method of inducing analgesia because bupivacaine has been known to cause systemic cardiovascular effects, e.g., arrhythmia, ventricular fibrillation, cardiac arrest, and more importantly, ibutilide is an agent known for its antiarrhythmic properties. Hence, the motivation to employ a known antiarrhythmic agent, ibutilide herein is seen.

Applicant's testing data of the working examples shown in Table 1-3 of the specification at pages 14-16 herein have been fully considered but are not deemed persuasive as to the nonobviousness and/or unexpected results of the claimed invention over the prior art since Table 1-3 merely demonstrates the particular agents, Ibutilide or sotalol (the only two particular methanesulfonamide compounds) in the particular amount, enhancing the local anesthetic potency of bupivacaine (the only one particular amide-linked or ester linked local anesthetic agent) in the particular amount, containing 1:200,000 epinephrine in a composition within the instant claims. Thus, the evidence in the examples is also not commensurate in scope with the claimed invention and does not demonstrate criticality of a claimed range of any methanesulfonamide compounds and any amide-linked or ester linked local anesthetic agents, encompassed in the claims herein, and any possible amounts of these agents to be administered for increasing the potency of local anesthetic. See MPEP § 716.02(d).

Moreover, note that the specification provides no side-by-side comparison with the closest prior art in support of nonobviousness for the instant claimed invention over the prior art. Note that arguments of counsel cannot take the place of factually supported objective evidence. See, e.g., *In re Huang*, 100 F.3d 135, 139-40, 40 USPQ2d 1685, 1689 (Fed. Cir. 1996); *In re De Blauwe*, 736 F.2d 699, 705, 222 USPQ 191, 196 (Fed. Cir. 1984).

Therefore, the evidence presented in specification herein is not seen to be clear and convincing in support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

It is merely noted for the record that the recitation "E4031" in claims 6 and 12 renders the claim(s) unclear as to "E4031" encompassed by the claims.

In view of the rejections to the pending claims set forth above, no claims are allowed.

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is

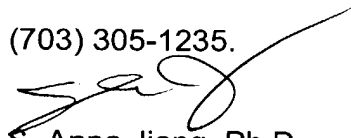
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(571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 703.872.9307.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 305-1235.



S. Anna Jiang, Ph.D.  
Patent Examiner, AU 1617  
March 9, 2004